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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,962	10/04/2004	Klaus Braun	4121-170	8435

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INTELLECTUAL PROPERTY / TECHNOLOGY LAW
PO BOX 14329
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EXAMINER	
MCGARRY, SEAN	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,962	BRAUN ET AL.	
	Examiner	Art Unit	
	Sean R. McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *15-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/23/05, 10/14/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I and SEQ ID NO: 25 in the reply filed on 12/22/06 is acknowledged. The traversal is on the ground(s) that all the peptides in claim 5 belong to the same class of peptides and that all of the claims [of groups I and II] share a common technical feature. It is noted that a discussion of a common technical feature is not needed since any special technical feature has been destroyed by virtue of the many prior at rejection set forth below.

The requirement is still deemed proper and is therefore made FINAL.

Claims 15-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/22/06.

Information Disclosure Statement

The information disclosure statement filed 10/14/04 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the references referred to as

"AA", "AD", and "AG" are in a language other than English. It is noted that the IDS indicates that all references provided, those that are in English or not in English, have been indicated to have been translated, however, no translations of the above cited references can be found in the IFW. It has been placed in the application file, but the information referred to therein as "AA", "AD", and "AG" have not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. This application fails to comply with at least 37 CFR 1.821(d). The specification and drawings contain nucleic acid and amino acid sequences that are not accompanied by the required sequence identifier. Applicant

should carefully review the application and ensure that it complies with the sequence rules.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 recites ". . .for which the prokaryote was re-sensitized by administering the conjugate." There is no antecedent basis for this language in the context of the claims.

Priority

Applicant cannot rely upon the foreign priority papers to overcome any rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 13 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Good et al. [Nature Biotechnology Vol. 19:360-364, April 2001].

Good et al have disclosed bactericidal peptide PNA conjugates. The conjugates comprise a peptide that that penetrates the cell membrane of E. coli and a PNA that inhibits *acpP* mRNA expression. The peptide and PNA are covalently linked.

Claims 1-4, 7-9, 13, 14, 18, and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by Nielsen et al [US 6,548,651].

Nielsen et al disclose modified PNA molecules that are conjugated to cationic peptides in order to enhance the anti-infective properties of the PNA. Nielson et al disclose that PNAs are advantageously used antisense compounds for microorganisms such as E. Coli (columns 2-3). The general formula of peptide-linker-PNA is first disclosed at column 3, where the linker can be a linker or a chemical bond (see column 6, for example). At column 7 many peptides are disclosed including magainins. It is disclosed at column 4 that the compounds can be used to inhibit infections by antibiotic

resistant bacteria. At column 8 it is disclosed that the PNA is targeted to targets responsible for resistance to antibiotics and includes a gene encoding beta-lactamase, for example (column 9). At column 8 many linkers are disclosed for use in their invention. At column 15 it is disclosed the combination of PNA conjugates and antibiotics for the treatment of infections.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-14, 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nielsen et al(supra), Good et al (supra) and Rothbard et al [WO 98/52614], in view of Bernhardt et al [Research in Microbiology Vol. 153:493-501, 2002]

and Yu et al [cited on applicant IDS filed 10/14/2004], Good et al (2)[Nature Biotechnology, Vol. 16:355-358], and Braun et al [US 6,821,948].

The claimed invention is as clearly set forth in the claims listed above. In general the invention is a PNA-transport conjugate for the inhibition of bacterial gene expression.

Nielsen et al disclose modified PNA molecules that are conjugated to cationic peptides in order to enhance the anti-infective properties of the PNA. Neilson et al disclose that PNAs are advantageously used antisense compounds for microorganisms such as E. Coli (columns 2-3). The general formula of peptide-linker-PNA is first disclosed at column 3, where the linker can be a linker or a chemical bond (see column 6, for example). At column 7 many peptides are disclosed including magainins which are antibacterial peptide, for example. It is disclosed at column 4 that the compounds of their invention can be used to inhibit infections by antibiotic resistant bacteria. At column 8 it is disclosed that the PNA is targeted to targets responsible for resistance to antibiotics and includes a gene encoding beta-lactamase that effect tolerance or susceptibility to ampicillin, for example, (column 9). At column 8 many linkers are disclosed for use in their invention. At column 15 it is disclosed the combination of PNA conjugates and antibiotics for the treatment of infections.

Good et al have disclosed bactericidal peptide PNA conjugates. The conjugates comprise a peptide that that penetrates the cell membrane of E. coli and a PNA that inhibits *acpP* mRNA expression. The peptide and PNA are covalently linked. At page 361 Good et al assert that the E. coli outer cell wall is a major barrier to PNAs and that

bacteria are permeabilized by cationic antimicrobial peptides and that such compounds can act synergistically with antimicrobials that enter cells poorly. Good et al tested whether such compound covalently attached to a PNA could further improve cell entry and found that indeed such antimicrobial peptides do indeed enhance PNA uptake into bacterial cells.

Rothbard et al have taught general teaching for the construction of compounds that enhance transport across biological membranes. At page three it is taught that the transport facilitator can be a peptide and at pages 4, 17, 21-22, and 34 for example, it is taught that biologically active agents such as PNAs can be facilitated across prokaryotic cell walls and membranes. At pages 4, 9, and 12-13 it is taught that various linkers such as cleavable linkers (including disulfide groups can be used to attach the transport moiety to the active agent. At page 26 it is disclosed the formulation of compounds with pharmaceutical carriers, for example. See also claims 13, 14, 15, 21, 22 and 24.

The prior art discussed so far has taught all of the limitations of the instant invention except the use of phage-holin and defensin peptides as transport mediators, the use of polylysine linkers, and the specific PNA sequence of claim 12.

Bernhardt et al and Yu et al are relied upon to show that phage-holin and defensin polypeptides were know at the time of invention and were known to be antimicrobial cell membrane penetrating polypeptides.

Good et al (2) is have taught the inhibition of beta-lactamase via PNA antisense molecules. It is noted that the antisense of Good et al is targeted to the beta-lactamase gene on the plasmid vector pBR322. The instant SEQ ID NO: 1 is also targeted to the

beta-lactamase gene of pBR322. The sequence of SEQ ID NO: 1 was conveniently chosen by applicant to perform the same known function of inhibiting the same beta-lactamase gene of pBR322.

Braun et al disclose the use of polylysine linkers in conjugates for cell membrane transport (see column 3, for example).

The prior art has clearly demonstrated the successful use of PNA molecules conjugated to cell penetrating moieties including bactericidal peptide transporter,. Since the art has taught the benefit of such compositions and the prior art has taught that any bactericidal cationic peptide could be used, it would be obvious to choose any of the known bactericidal peptides known to permeate prokaryotic cell membranes (as was suggested by Good et al). The prior art provides a quantity of guidance on the choice of linkers one may choose or making the compounds of the invention (ie conjugates for cell membrane transport). One would clearly have been motivated to make the claimed conjugates since the prior art has made it abundantly clear that PNA activity is enhanced via the conjugation to cell membrane transporting moieties.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R. McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on (571) 272-0763. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sean R McGarry
Primary Examiner
Art Unit 1635